

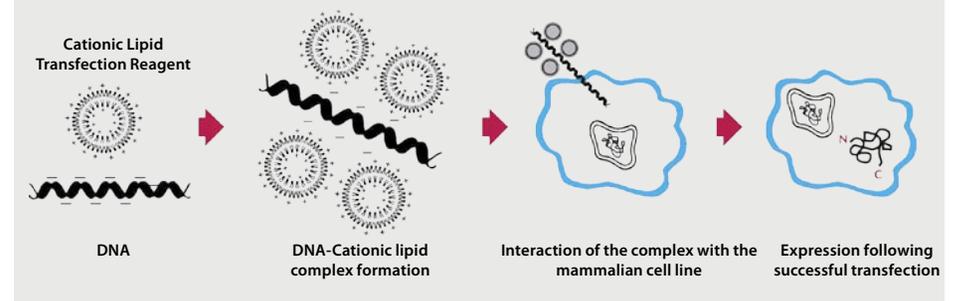
Mechanism of cationic lipid-mediated transfection

Specially designed cationic lipids, such as Lipofectamine™ 2000 Transfection Reagent, facilitate DNA and siRNA delivery into cells (1–3). The basic structure of cationic lipids consists of a positively charged head group and one or two hydrocarbon chains. The charged head group governs the interaction between the lipid and the phosphate backbone of the nucleic acid, and facilitates DNA condensation. Often cationic lipids are formulated with a neutral co-lipid or helper lipid, followed by extrusion or microfluidization, which results in a unilamellar liposomal structure with a positive surface charge when formulated in water.

The positive surface charge of the liposomes also mediates the interaction of the nucleic acid and the cell membrane, allowing for fusion of the liposome/nucleic acid (“transfection complex”) with the negatively charged cell membrane. The transfection complex is thought to enter the cell through endocytosis. Endocytosis is the process where a localized region of the cellular membrane uptakes the DNA: liposome complex by forming a membrane bound/intracellular vesicle. Once inside the cell, the complex must escape the endosomal pathway, diffuse through the cytoplasm, and enter the nucleus for gene expression. Cationic lipids are thought to facilitate transfection during the early steps of the process by mediating DNA condensation and DNA/cellular interactions.

The principle of delivery using cationic lipid reagents thus differs from prior attempts to use neutral liposomes for transfections. With cationic lipid reagents, the DNA solution is not deliberately encapsulated within the liposomes, rather, the negatively charged DNA binds spontaneously to the positively charged liposomes, forming DNA-cationic lipid reagent complexes (Figure 1)

Figure 1—General lipid design and proposed mechanism for DNA entry into cells



Some of the problems associated with traditional transfection methods like calcium phosphate coprecipitation, DEAE-dextran, polybrene and electroporation, include low efficiency of DNA delivery, poor reproducibility, cell toxicity, and inconvenience. However, cationic lipid reagent-mediated transfection yields high and previously unattainable transfection efficiencies in a wide variety of eukaryotic cells. It is simple to perform, and ensures consistently reproducible results. Moreover, a number of cell lines normally resistant to transfection by other methods transfect successfully using cationic lipid reagents.

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3. Liu, D. *et al.* (2003) *Current Medicinal Chemistry* **10**: 1307-1315.

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